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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,850	12/14/2001	Patrick M. Hughes	D-3004	7435

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 05/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,850	HUGHES ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 14-16* is/are pending in the application.

4a) Of the above claim(s) *7 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8, 9, 11, 12 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' Request for Continued Examination (RCE) filed February 18, 2005 is acknowledged and accepted. Claim 13 is canceled. Claims 1-12 and 14-16 are pending wherein the therapeutic component is a quinoxaline compound. Claims 7 and 10 remain withdrawn from consideration by the Examiner, 37 CFR 1.142(b), as directed to non-elected inventions. The subject matter presently under consideration remains those topical ophthalmic compositions of claims 1-6, 8, 9, 11, 12, 14-16, wherein the therapeutic component is a quinoxaline compound of instant claim 8.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 8, 9, 11, 12, 14-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-10 and 32-34 of U.S. Patent No. 6562873. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed subject matter of U.S. Patent 6,562,873 encompasses that of instant claims in that alpha-2 adrenergic agonists may be therapeutic components. A "composition" encompasses a conjugate.

The open language of the present claims allows for the inclusion of additional active agents.

Claims 1-6, 8, 9 and 11-16 were rejected under 35 U.S.C. 112, second paragraph, in the last Office Action as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention with respect to the term "general" in the description of formula A.

Subsequent to the deletion of the term, this rejection of record is withdrawn.

In the last Office Action claims 1-6, 8, 9 and 11-16 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It was asserted the instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation.

Applicants argue, taken as a whole, the present specification discloses sufficient information to enable a person of ordinary skill in the art to make and use the claimed topical ophthalmic compositions, as ophthalmic drops.

Applicants' arguments are persuasive and the rejection of record under 35 U.S.C. 112, first paragraph, is withdrawn.

Claim 8 was rejected in the last Office Action under 35 U.S.C. 112, both first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make the invention, and for

failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. It was asserted the cited examples on pages 9-10 are precisely quinoxaline, not derivatives.

The rejection of claim 8 is withdrawn following the deletion of the term "derivatives".

Claims 1-6, 8, 9, 11-13, 15 and 16 were rejected under 35 U.S.C. 103(a) as being unpatentable over both Desantis, L., US 2001/0047012, and Collins et al., WO 01/92288, in the last Office Action. It was asserted Desantis teaches combination therapy for treating glaucoma comprising administering a glutamate antagonist and an intraocular pressure-lowering compound. Brimonidine, 5-bromo-N-(4,5-dihydro-1H-imidazole-2-yl)-6-quinoxalinamine, a compound of instant claim 8, is a preferred intraocular pressure-lowering compound and memantine is a well established glutamate antagonist. See page 2, paragraphs [0018] and [0023]. Application to the eye encompasses topical administration. Collins teaches various pharmaceutical conjugates comprising a bioactive agent that is covalently bound directly or indirectly to a linker. Efficacy enhancing components of formula A are disclosed on page 92. Therefore, in view of the combined teachings of Desantis and Collins, one skilled in the art of formulation chemistry who seeks a pharmaceutical conjugate comprising a therapeutic component and an efficacy enhancing component of instant formula A would have been motivated to prepare a formulation comprising two known therapeutically effective ophthalmic agents in a formulation that is a conjugate to treat ocular pathologies.

Applicants argue there is no motivation provided to combine the teachings of the references to obtain the claimed conjugates. Applicants urge the agents are separate from each other in the Desantis reference. In the Collins reference Applicants argue amantadine is disclosed to be a therapeutic component, not an efficacy-enhancing component, while the efficacy-enhancing component has a completely different chemical structure.

Applicants' arguments have been given careful consideration but are not found persuasive. The rejection of claims 1-6, 8, 9, 11, 12, 15 and 16 is repeated for the reasons of record.

1-Aminoadamantane analogues, such as memantine, are established in the prior art as useful agents for conjugation with poorly soluble drugs. Such conjugates provide chemical stability and are known to dissociate under physiological conditions. Desantis establishes a therapeutic advantage of combining known ophthalmic drugs such as memantine and brimonidine. Collins teaches pharmaceutical conjugates with a low molecular weight linker to which a bioactive agent may be covalently bound. The intended uses, as defined in claim 1 as "a therapeutic component" and "an efficacy enhancing component", confer no patentable weight to composition claims. The applied references teach the combination of a compound of instant formula A with various therapeutic agents. The specification fails to define a "conjugate" as anything more than a combination of compounds wherein increased solubility or bioavailabilty is sought.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached Mondays to Fridays from 10:30 AM to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Chris Low, can be reached at telephone number 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

PHYLLIS SPIVACK
PRIMARY EXAMINER

April 30, 2005